DYSPROTEINEMIA IN THE CHRONIC DERMATOMYCOSIS DUE TO *T. RUBRUM* WITH NEGATIVE ANERGY TO TRICHOPHYTIN*

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Although a considerable body of information has been gathered on alterations in the serum proteins in some systemic infections (1), similar information in the instance of skin infections is as yet inadequate. No reports on the patterns of serum proteins in patients with chronic, superficial fungous infections of the skin have been published to our knowledge. Our interest in this subject was aroused on reviewing a survey on the nature of trichophytin reactivity in patients with *T. rubrum* infections. Out of more than 250 trichophytin tests carried out on these patients, we came across 8 cases who had recalcitrant, chronic, generalized dermatomycosis and who showed negative immediate and delayed trichophytin reactions (Fig. 1a and c). These patients had never been free of the disease for a period varying from one to twelve years. These findings may be akin to the absence of specific cutaneous reactivity indicating negative anergy reported in the subjects of systemic fatal coccidioidomycosis and histoplasmosis (2). Similarly negative tuberculin reactions in cases of fatal miliary tuberculosis are also well-known. Since it is known that there is a lack of resistance to systemic bacterial and viral infections in the subjects with hypo- and agammaglobulinemia (3), we thought it worthwhile to investigate the patterns of serum proteins of these cases and find out if these defects existed in them.

MATERIAL AND METHODS

Estimations of serum protein fractions were carried out by the Tisselius procedure of electrophoresis, and the total proteins were estimated by the Biuret method. The fractionations of the serum proteins were carried out as advocated by Gronwall (4). In this procedure, strips of treated filter paper were processed in the standard phenobarbitone buffer for four hours after which they were dried in an oven at 100° C, and stained with 1% bromphenol-blue in a saturated alcoholic solution of mercuric chloride. The five protein-fractions could then be visually delineated on the strips (Fig. 1b), which were cut at the points of demarcations between them. The dye from each strip was eluted in a 5 per cent sodium carbonate solution in 50 per cent methanol. The density of the dye in the eluted solution from each fraction was measured by the spectrophotometer and it was assumed that the amount of dye was proportional to the amount of proteins in each strip. Quantity of each fraction was then obtained by computing the product of the per cent of the dye in the respective strips, and the quantity of the total proteins obtained by the Biuret method. The standardization of the above procedure was established on a large number of normal and abnormal sera by the department of biochemistry.

Table I shows the serum protein patterns and the duration of the disease of the above 8 subjects. These are compared with the values derived from a report concerning 187 normal subjects published from our institution (5). It should be mentioned that the "normal" values of the gamma-globulins in the Indian subjects are known to be about 20 per cent higher and they probably express a diet which is poor in animal proteins as well as a higher incidence of infective disorders.

As compared to the normal patterns, every patient showed the total proteins near the upper-normal range or more, consistent hypoalbuminemia, an increase in the alpha-1 globulins (except in one), higher values or increase in the alpha-2 globulins and an increase in the gamma globulins. The latter were markedly elevated in all, and above 2 gram per cent in seven subjects. The beta globulins were increased in only two subjects (Nos. VI and VIII).

Identical patterns of disturbed serum proteins in our subjects are reported in the chronic infective states such as kala-azar, leprosy, chronic tuberculosis, chronic amoebiasis, and also in the cirrhosis of liver, Hodgkin's disease and multiple myeloma. None of our patients showed evidences of these diseases on subsequent investigations.

DISCUSSION AND SUMMARY

The findings of abnormally high values in alpha-1, alpha-2 and gamma globulins instead of hypo-and agammaglobulinemia resulting in a pronounced dysproteinemia were unexpected. However, some corroboration of our results are available in the literature. Thus similar dysproteinemia is recorded in the isolated reports of recalcitrant fungous infections of the skin, when this investigation was carried out. Recently Engle (6) published a case of disseminated monilial granulomas with hypergammaglobulinemia. Although his patient also had hypoalbuminemia as well as

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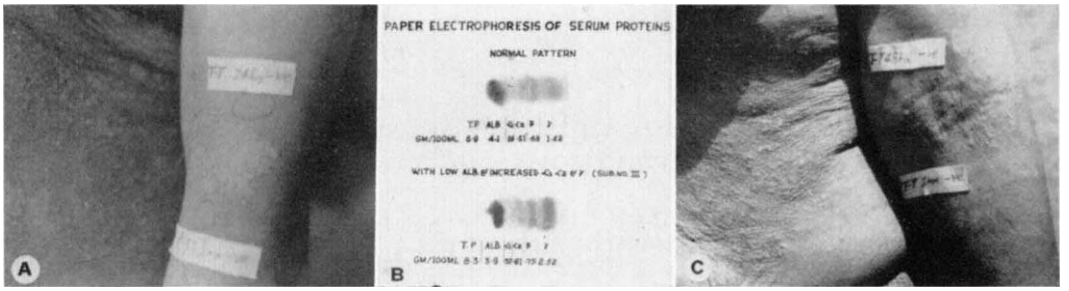

FIG. 1a and c.: Two patients with generalized *T. rubrum* infections showing negative trichophytin anergy.
FIG. 1b.: Electrophoretic strips showing a normal and an abnormal pattern.

TABLE I

Serum proteins in chronic dermatomycosis due to T. Rubrum with negative trichophytin tests

Subject No.	Duration of Disease	Total Proteins	Patterns of Serum Proteins				
			Albumin	Globulins			
				Alpha-1	Alpha-2	Beta	Gamma
I	12 years	7.4	2.97 (40.4)	0.32 (4.3)	0.61 (8.3)	0.64 (8.7)	2.82 (38.3)
II	1 year	7.8	3.60 (46.2)	0.15 (1.9)	0.55 (7.1)	0.65 (8.3)	2.85 (36.5)
III	2 years	8.3	3.9 (47.0)	0.32 (3.9)	0.81 (9.8)	0.75 (9.0)	2.52 (30.4)
IV	1½ years	8.0	2.87 (35.9)	0.34 (4.3)	0.84 (10.3)	0.70 (8.8	3.25 (40.6)
V	5 years	6.0	2.07 (34.5)	0.34 (5.7)	0.69 (11.5)	0.76 (12.7)	2.14 (35.7)
VI	1 year	7.5	3.37 (44.9)	0.44 (5.9)	0.57 (7.6)	1.06 (14.1)	2.06 (27.5)
VII	1 year	7.5	3.77 (50.3)	0.38 (5.1)	0.91 (12.1)	0.72 (9.6)	1.72 (22.9)
VIII	2½ years	7.1	3.03 (42.7)	0.32 (4.5)	0.65 (9.2)	0.91 (12.8)	2.19 (30.8)
Indian normals	187 subjects	6.86 ±0.37	4.47 ±0.38	0.15 ±0.06	0.43 ±0.11	0.65 ±0.14	1.16 ±0.28

Note: The figures express the absolute values in gram per cent and those in the brackets are the percentage of each fraction compared to the total proteins.

raised alpha-1 and alpha-2 globulins compared with the American normals, he did not interpret the latter as abnormal and mentioned only about the gammaglobulins. Blank's (7) unique case of extensive cutaneous and subcutaneous granulomatous lesions due to *T. rubrum* also had similar alterations in the serum proteins. Again one of the six cases with recalcitrant and severe *T. rubrum* infections associated with malignant lymphoma reported by Lewis *et al.* (8) had hyperglobulinemia and hypoalbuminemia. Since electrophoretic methods were not employed, the values of the globulin fractions are not known. Extending this experience to other chronic cutaneous infections, we found exactly similar patterns of disturbed serum proteins in 13 subjects of chronic, recurrent, deep folliculitis, and other types of chronic pyoderma which were resistant to the antibacterial therapy (9). These findings raise the issue of whether dysproteinemia (including hypergammaglobulinemia) is the "result" or the "cause" underlying a lack of resistance to the microbial invaders, and leaves unresolved the question of the exact nature of this defect.

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